

PRELIMINARY AMENDMENT

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hydroxyethyl cellulose and sodium carboxymethyl cellulose  
and

(iii) one or more of a water-absorbing and water-insoluble base material selected from the group consisting of crystalline cellulose,  $\alpha$ -cellulose, cross-linked sodium carboxy-methyl cellulose, cross-linked starch, gelatin, casein, tragacanth gum, polyvinyl pyrrolidone, chitin and chitosan,

(2) the content of the water-soluble and gel-forming base material is about 5-40 wt % based on the total of the water-absorbing and water-insoluble base material and the water-absorbing and gel-forming base material, and

(3) the drug is unevenly dispersed more on/in the water-absorbing and water-insoluble base material than on/in the water-absorbing and gel-forming base material.

20. A powdery composition for nasal administration described in

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Claim 19, wherein the state in which the drug is unevenly dispersed more ~~on/in~~ <sup>on or in</sup> the water-absorbing and water-insoluble base material than ~~on/in~~ <sup>on or in</sup> the water-absorbing and gel-forming base material is obtainable by a method that the drug is vigorously mechanically mixed with the water-absorbing and water-insoluble base material, in which at least 90 wt % based on the particles

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have an average particle diameter in the range of 10-350  $\mu\text{m}$ , subsequently, the water-absorbing and gel-forming base material, in which at least 90 wt % based on the particles have an average particle diameter in the range of 10-350  $\mu\text{m}$ , is mechanically mixed with the resultant mixture.

C 21. A powdery composition for nasal administration described in Claim 19, wherein the powdery composition is obtainable by a method that the drug is allowed to adhere to the water-absorbing and water-insoluble base material by freeze drying, then, the water-absorbing and water-insoluble base material with the adhered drug is pulverized and sieved so that at least 90 wt % based on the resultant particles have an average particle diameter in the range of 10-350  $\mu\text{m}$ , subsequently, the water-absorbing and gel-forming base material, in which at least 90 wt % based on the particles have an average particle diameter in the range of 10-350  $\mu\text{m}$ , is mechanically mixed with the resultant water-absorbing and water-insoluble base material.

22. A powdery composition for nasal administration described in Claim 19, wherein the powdery composition is obtainable by a method that the drug and the water-absorbing and water-insoluble base material are dissolved or dispersed in an organic solvent, and subsequently the resultant solution or dispersion is

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evaporated such that a powder is obtained, further the powder is pulverized and sieved such that at least 90 wt% based on the resultant particles have an average particle diameter in the range of 10-350  $\mu\text{m}$ , and the water-absorbing and gel-forming base material, in which at least 90 wt% based on the particles have an average particle diameter in the range of 10-350  $\mu\text{m}$ , is mechanically mixed with the resultant powder.

23. A powdery composition for nasal administration described in Claim 19, wherein the state in which the drug is dispersed more *on or in* the water-absorbing and water-insoluble base material than *on or in* the water-absorbing and gel-forming base material is *obtainable* by making the average particle diameter of the water-absorbing and water-insoluble base material larger than that of the water-absorbing and gel-forming base material.

sub 24. A powdery composition for nasal administration described in Claim 23, wherein the water-absorbing and water-insoluble base material has an average particle diameter of 10-350  $\mu\text{m}$  in at least 90 wt % based on the particles, and the water-absorbing and gel-forming base material has an average particle diameter of 10-105  $\mu\text{m}$  in at least 90 wt % based on the particles.

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25. A powdery composition for nasal administration described in Claim 23, wherein the water-absorbing and water-insoluble base material has an average particle diameter of 10-250  $\mu\text{m}$  in at least 90 wt% based on the particles, and the water-absorbing and gel-forming base material has an average particle diameter of 10-65  $\mu\text{m}$  in at least 90 wt% based on the particles.

26. A powdery composition for nasal administration described in any one of Claim 19 to Claim 23, wherein the drug is selected from the group consisting of non-peptide/non-proteinaceous drugs and peptide/proteinaceous drugs having molecular weight of 30,000 or less.

27. A powdery composition for nasal administration described in Claim 26, wherein the non-peptide/non-proteinaceous drug is one or more drugs selected from the group consisting of anti-inflammatory/steroids, nonsteroidal anti-inflammatory drugs, analgesic anti-inflammatory agents, antitussive expectorants, antihistaminic agents, antiallergic drugs, antiemetic drugs, hypnotics, vitamin preparations, sex steroid hormones, antineoplastic drugs, antiarrhythmic drugs, antihypertensive drugs, antianxiety drugs, psychotropic drugs, antiulcer drugs, cardiotonics, analgesics, bronchodilators, treating agents for obesity, antithrombotic drugs, antidiabetic drugs, muscle relaxants and anti-rheumatics.

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28. A powdery composition for nasal administration described in Claim 26, wherein the peptide/proteinaceous drug is one or more drugs selected from the group consisting of luteinizing hormone-releasing hormones, growth hormone-releasing factors, somatostatin derivatives, vasopressins, oxytocins, hirudin derivatives, enkephalins, adrenocorticotrophic hormone derivatives, bradykinin derivatives, calcitonins, insulins, glucagon derivatives, growth hormones, growth hormone-releasing hormones, luteinizing hormones, insulin-like growth factors, calcitonin gene-related peptides, atrial natriuretic polypeptide derivatives, interferons, erythropoietin, granulocyte colony forming-stimulating factor, macrophage forming-stimulating factor, parathyroid hormones, parathyroid hormone-releasing hormone, prolactin, thyroid-stimulating hormone-releasing hormone and angiotensins.

29. A powdery composition for nasal administration described in any one of Claim 19 to Claim 23, wherein the drug is a peptide/proteinaceous drug having a molecular weight of 500-1500, and the amount of the water-absorbing and gel-forming base material is about 5-30 wt % based on the total of the water-absorbing and water-insoluble base material and the water-absorbing and gel-forming base material.

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30. A powdery composition for nasal administration described in Claim 29, wherein the peptide/proteinaceous drug is one or more drugs selected from the group consisting of vasopressins, luteinizing hormone-releasing hormones, growth hormone-releasing factors, somatostatin derivatives, oxytocins, hirudin derivatives, enkephalins, adrenocorticotrophic hormone derivatives and bradykinin derivatives.

31. A powdery composition for nasal administration described in any one claim among Claim 19 to Claim 23, wherein the drug is a peptide/proteinaceous drug having a molecular weight of 1500-30,000 and the amount of the water-absorbing and gel-forming base material is about 5-20 wt % based on the total of the water-absorbing and water-insoluble base material and the water-absorbing and gel-forming base material.

32. A powdery composition for nasal administration described in Claim 31, wherein the peptide/proteinaceous drug is one or more drugs selected from the group consisting of calcitonins, insulins, glucagon derivatives, growth hormones, growth hormone-releasing hormones, luteinizing hormones, insulin-like growth factors, calcitonin gene-related peptides, atrial natriuretic polypeptide derivatives, interferons, erythropoietin, granulocyte colony-stimulating factor, macrophage-

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stimulating factor, parathyroid hormones, parathyroid hormone-releasing hormone, prolactin, thyroid-stimulating hormone-releasing hormone and angiotensins.

33. A powdery composition for nasal administration described in any one of Claim 19 to Claim 32, wherein the water-absorbing and water-insoluble base material is one or more materials selected from the group consisting of crystalline cellulose,  $\alpha$ -cellulose, cross-linked sodium carboxymethyl cellulose, cross-linked starch, gelatin, casein, tragacanth gum, polyvinyl pyrrolidone, chitin and chitosan.

C 34. A powdery composition for nasal administration described in any one of Claim 19 to Claim <sup>25</sup>32, wherein the water-absorbing and water-insoluble base material is crystalline cellulose.

35. A powdery composition for nasal administration described in any one of Claim 19 to Claim 32, wherein the water-absorbing and gel-forming base material is one or more materials selected from the group consisting of hydroxypropyl cellulose, hydroxypropylmethyl cellulose, methyl cellulose and sodium carboxymethyl cellulose.

C 36. A powdery composition for nasal administration described in any one of Claim 19 to Claim <sup>25</sup>32, wherein the water-absorbing and gel-forming base

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material is hydroxypropyl cellulose.

37. A powdery composition for nasal administration described in Claim 36, wherein the hydroxypropyl cellulose has a viscosity of 150-4000 cps in 2% aqueous solution.

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38. A powdery composition for nasal administration described in Claim 19, wherein the state in which the drug is unevenly dispersed more *on or in* the water-absorbing and water-insoluble base material than *on or in* the water-absorbing and gel-forming base material is achieved by mechanically mixing the drug with the water-absorbing and water-insoluble base material, subsequently, adding the water-absorbing and gel-forming base material to the resultant mixture, and mechanically mixing thereof.

39. A powdery composition for nasal administration described in Claim 38, wherein the mechanically mixing the drug with the water-absorbing and water-insoluble base material drug is vigorously mechanically mixing.

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40. A powdery composition for nasal administration described in Claim 19, wherein the state in which the drug is unevenly dispersed more *on or in* the water-absorbing and water-insoluble base material than *on or in* the water-absorbing and gel-forming base material is achieved by dissolving or dispersing the drug and the water-absorbing and water-insoluble base material in an aqueous solution, freeze drying the resultant solution for obtaining the drug-adhered to the water-absorbing and water-insoluble base material, pulverizing and sieving the resultant drug-adhered to the water-absorbing and water-insoluble base material for obtaining a



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powder fraction, adding the water-absorbing and gel-forming base material to the powder fraction, and mechanically mixing thereof.

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41. A powdery composition for nasal administration described in Claim 40, wherein the state in which the drug is unevenly dispersed more ~~on~~ <sup>on or in</sup> the water-absorbing and water-insoluble base material than ~~on~~ <sup>on or in</sup> the water-absorbing and gel-forming base material is achieved by dissolving or dispersing the drug and the water-absorbing and water-insoluble base material in an organic solvent, evaporating the resultant solution for obtaining the drug-adhered to the water-absorbing and water-insoluble base material, pulverizing and sieving the resultant drug-adhered to the water-absorbing and water-insoluble base material for obtaining a powder fraction, adding the water-absorbing and gel-forming base material to the powder fraction, and mechanically mixing thereof.

42. A powdery composition for nasal administration described in any one of claims 38 to 41, wherein average particle diameters of the water-absorbing and water-insoluble base material and the water-absorbing and gel-forming base material is at least 90 wt % based on the particles in the range of 10-350 <sup>um</sup> ~~m~~.

43. A powdery composition for nasal administration described in claim 39, wherein average particle diameters of the water-absorbing and water-insoluble base material and the water-absorbing and gel-forming base material is at least 90 wt % based on the particles in the range of 10-350 <sup>um</sup> ~~m~~.

44. A powdery composition for nasal administration described in claim 40, wherein average particle diameters of the water-absorbing and water-insoluble